



MT-TH gene

mitochondrially encoded tRNA histidine

Normal Function

The *MT-TH* gene provides instructions for making a particular type of RNA, a molecule that is a chemical cousin of DNA. This type of RNA, called transfer RNA (tRNA), helps assemble protein building blocks known as amino acids into full-length, functioning proteins. The *MT-TH* gene provides instructions for a specific form of tRNA that is designated as tRNA^{His}. During protein assembly, this molecule attaches to a particular amino acid, histidine (His), and inserts it into the appropriate locations in the growing protein.

The tRNA^{His} molecule is present in cellular structures called mitochondria. These structures convert energy from food into a form that cells can use. Through a process called oxidative phosphorylation, mitochondria use oxygen, simple sugars, and fatty acids to create adenosine triphosphate (ATP), the cell's main energy source. The tRNA^{His} molecule is involved in the assembly of proteins that carry out oxidative phosphorylation.

Health Conditions Related to Genetic Changes

mitochondrial encephalomyopathy, lactic acidosis, and stroke-like episodes

A small number of people with the features of mitochondrial encephalomyopathy, lactic acidosis, and stroke-like episodes (MELAS) have a mutation in the *MT-TH* gene. This condition is characterized by recurrent severe headaches, muscle weakness (myopathy), hearing loss, stroke-like episodes including a loss of consciousness, seizures, and other problems affecting the nervous system. Some people with an *MT-TH* gene mutation also have features of another mitochondrial disorder called myoclonic epilepsy with ragged-red fibers (MERRF); these additional features can include muscle twitches (myoclonus), difficulty coordinating movement (ataxia), and abnormal muscle cells known as ragged-red fibers. This combination of signs and symptoms is called MERRF/MELAS overlap syndrome.

MT-TH gene mutations that cause MELAS and MERRF/MELAS overlap syndrome change single DNA building blocks (nucleotides) in the gene. Researchers have not determined how these genetic changes alter energy production in mitochondria or cause the varied signs and symptoms of MELAS or MERRF/MELAS overlap syndrome.

myoclonic epilepsy with ragged-red fibers

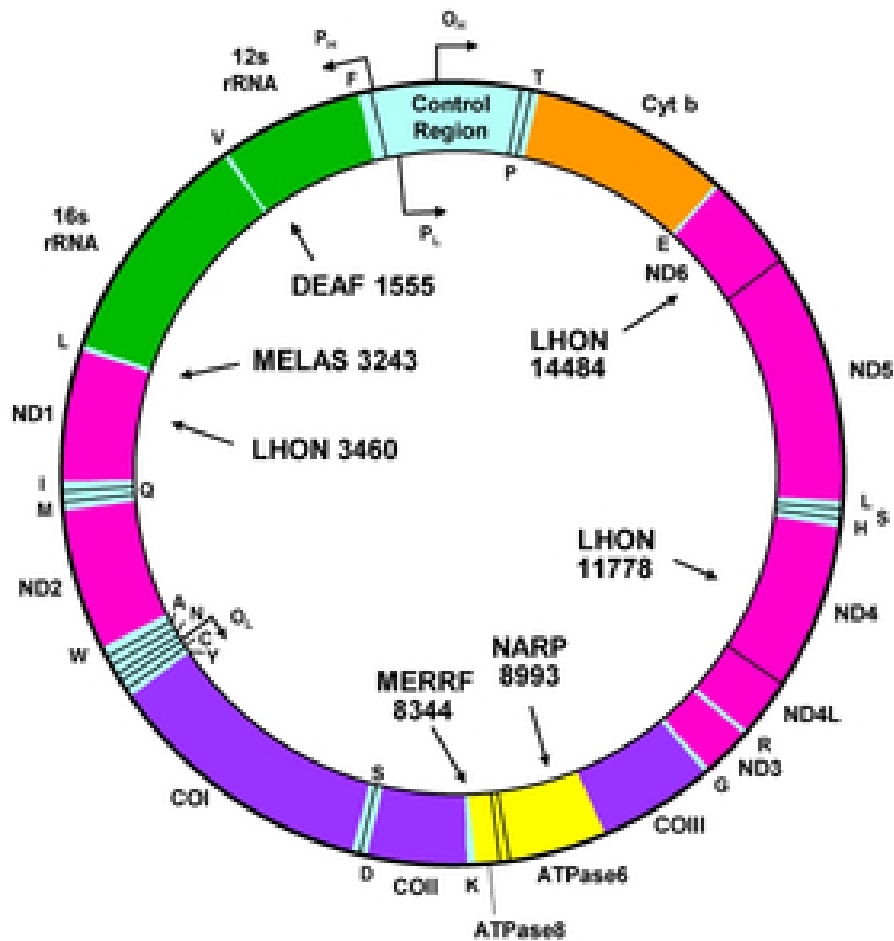
As mentioned above, a few individuals with a mutation in the *MT-TH* gene have features of both myoclonic epilepsy with ragged-red fibers (MERRF) and MELAS. The mutation involved in this overlap syndrome replaces the nucleotide guanine with the nucleotide adenine at gene position 12147 (written as G12147A). It remains unknown why this mutation causes the overlapping features of MERRF and MELAS.

other disorders

Another mutation in the *MT-TH* gene may increase the risk of developing a heart condition called cardiomyopathy. People with cardiomyopathy have a weakened heart muscle that is unable to pump blood effectively. A particular change in the *MT-TH* gene has been identified in several adults with cardiomyopathy, but without other common signs of mitochondrial disease such as neurological abnormalities. This mutation replaces the nucleotide guanine with the nucleotide adenine at gene position 12192 (written as G12192A). It is unclear why this alteration in mitochondrial DNA may increase a person's risk of developing heart problems without affecting other parts of the body.

Chromosomal Location

Molecular Location: base pairs 12,138 to 12,206 on mitochondrial DNA (Homo sapiens Annotation Release 108, GRCh38.p7) (NCBI)



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Other Names for This Gene

- MTTH
- tRNA histidine

Additional Information & Resources

Educational Resources

- Basic Neurochemistry (sixth edition, 1999): Diseases of Mitochondrial Metabolism
<https://www.ncbi.nlm.nih.gov/books/NBK27914/>
- Madame Curie Bioscience Database: Mitochondrial Translation System
<https://www.ncbi.nlm.nih.gov/books/NBK6292/#A27945>
- Mayo Clinic Mitochondrial Disease Biobank
<http://www.mayo.edu/research/centers-programs/mitochondrial-disease-biobank/overview>
- Neuromuscular Disease Center, Washington University: MELAS
<http://neuromuscular.wustl.edu/mitosyn.html#melas>
- Neuromuscular Disease Center, Washington University: MERRF
<http://neuromuscular.wustl.edu/mitosyn.html#merrf>
- The Cell: A Molecular Approach (second edition, 2000): The Genetic System of Mitochondria
<https://www.ncbi.nlm.nih.gov/books/NBK9896/#A1629>

GeneReviews

- MELAS
<https://www.ncbi.nlm.nih.gov/books/NBK1233>
- MERRF
<https://www.ncbi.nlm.nih.gov/books/NBK1520>
- Mitochondrial Disorders Overview
<https://www.ncbi.nlm.nih.gov/books/NBK1224>

Scientific Articles on PubMed

- PubMed
<https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28MTTH%5BTIAB%5D%29+OR+%28tRNA+histidine%5BTIAB%5D%29%29+OR+%28%28G12147A%5BTIAB%5D%29+OR+%28G12192A%5BTIAB%5D%29%29+OR+%28tRNA%28His%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+3600+days%22%5Bdp%5D>

OMIM

- TRANSFER RNA, MITOCHONDRIAL, HISTIDINE
<http://omim.org/entry/590040>

Research Resources

- ClinVar
<https://www.ncbi.nlm.nih.gov/clinvar?term=MT-TH%5Bgene%5D>
- HGNC Gene Family: Mitochondrially encoded tRNAs
<http://www.genenames.org/cgi-bin/genefamilies/set/843>
- HGNC Gene Symbol Report
http://www.genenames.org/cgi-bin/gene_symbol_report?q=data/hgnc_data.php&hgnc_id=7487
- Mitomap: rRNA/tRNA mutations
<http://www.mitomap.org/MITOMAP/MutationsRNA>
- NCBI Gene
<https://www.ncbi.nlm.nih.gov/gene/4564>

Sources for This Summary

- Blakely EL, Yarham JW, Alston CL, Craig K, Poulton J, Brierley C, Park SM, Dean A, Xuereb JH, Anderson KN, Compston A, Allen C, Sharif S, Enevoldson P, Wilson M, Hammans SR, Turnbull DM, McFarland R, Taylor RW. Pathogenic mitochondrial tRNA point mutations: nine novel mutations affirm their importance as a cause of mitochondrial disease. *Hum Mutat.* 2013 Sep;34(9):1260-8. doi: 10.1002/humu.22358.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/23696415>
Free article on PubMed Central: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3884772/>
- Calvaruso MA, Willemssen MA, Rodenburg RJ, van den Brand M, Smeitink JA, Nijtmans L. New mitochondrial tRNA HIS mutation in a family with lactic acidosis and stroke-like episodes (MELAS). *Mitochondrion.* 2011 Sep;11(5):778-82. doi: 10.1016/j.mito.2011.06.004. Epub 2011 Jun 17.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/21704194>
- Finsterer J, Harbo HF, Baets J, Van Broeckhoven C, Di Donato S, Fontaine B, De Jonghe P, Lossos A, Lynch T, Mariotti C, Schöls L, Spinazzola A, Szolnoki Z, Tabrizi SJ, Tallaksen CM, Zeviani M, Burgunder JM, Gasser T; European Federation of Neurological Sciences. EFNS guidelines on the molecular diagnosis of mitochondrial disorders. *Eur J Neurol.* 2009 Dec;16(12):1255-64.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/19950421>
- Melone MA, Tessa A, Petrini S, Lus G, Sampaolo S, di Fede G, Santorelli FM, Cotrufo R. Revelation of a new mitochondrial DNA mutation (G12147A) in a MELAS/MERFF phenotype. *Arch Neurol.* 2004 Feb;61(2):269-72.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/14967777>
- Mimaki M, Ikota A, Sato A, Komaki H, Akanuma J, Nonaka I, Goto Y. A double mutation (G11778A and G12192A) in mitochondrial DNA associated with Leber's hereditary optic neuropathy and cardiomyopathy. *J Hum Genet.* 2003;48(1):47-50.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/12560876>

- Shin WS, Tanaka M, Suzuki J, Hemmi C, Toyo-oka T. A novel homoplasmic mutation in mtDNA with a single evolutionary origin as a risk factor for cardiomyopathy. *Am J Hum Genet.* 2000 Dec; 67(6):1617-20. Epub 2000 Oct 18.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/11038324>
Free article on PubMed Central: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1287941/>
 - OMIM: TRANSFER RNA, MITOCHONDRIAL, HISTIDINE
<http://omim.org/entry/590040>
 - Taylor RW, Schaefer AM, McDonnell MT, Petty RK, Thomas AM, Blakely EL, Hayes CM, McFarland R, Turnbull DM. Catastrophic presentation of mitochondrial disease due to a mutation in the tRNA(His) gene. *Neurology.* 2004 Apr 27;62(8):1420-3.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/15111688>
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